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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/928,102	08/10/2001	Thomas T. Perls	BIT-001(1538/47)	6355

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Patent Administrator
Testa, Hurwitz & Thibeault, LLP
125 High Street
High Street Tower
Boston, MA 02110

EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/18/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/928,102	Applicant(s) PERLS ET AL.	
	Examiner Carla Myers	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 November 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *12* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. This action is in response to the amendment filed October 2, 2002. Applicants arguments presented in the response of October 2, 2002 have been fully considered but are not persuasive to overcome all grounds of rejection. Any rejections not reiterated herein are hereby withdrawn. This action is made final.

THE FOLLOWING ARE NEWAND/OR MODIFIED GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS:

2. Claims 15-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for determining if an individual has an increased propensity for longevity, wherein the method comprises obtaining DNA from a first individual and DNA from a second individual who is at least 98 years of age; amplifying DNA from said first and second individuals to obtain an amplification product wherein the amplification product comprises the D4S1564 marker of human chromosome 4 and the amplified product contains nucleotide sequences within a region flanked by the genetic markers D4S1564 and D4S1572; comparing the amplified DNA product from the first and second individual, wherein when the amplified DNA product of the first individual is identical to that of the second individual, the first individual is identified as having an increased propensity for longevity, does not reasonably provide enablement for methods for determining a propensity for longevity wherein the methods comprise determining a propensity for longevity in a patient based upon **an identity** between a segment obtained from an individual at least 98 years of age and said patient, wherein said segment comprises a region flanked by the genetic markers D4S1564 and D4S1572. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn to methods for determining a propensity for longevity wherein the methods comprise comparing a DNA fragment flanked by the genetic markers D4S1564 and D4S1572 between a patient and an individual who is at least 98 years of age and determining that the first individual has a propensity based upon an identity between said segment from said patient and said individual who is at least 98 years of age. The specification provides the results of a study of 308 individuals belonging to 137 families in which at least one sibling was 98 years old and a second sibling was at least 95 years old (female) or 91 years old (male). Table 1 of the specification provides information regarding the results of a LOD score analysis between longevity and the following genetic markers: D4S1564 (MLS=3.65), D4S411 (MLS=3.07), D4S1572 (MLS=3.07), D4S2986 (MLS=2.78), and D4S406 (MLS=2.55). The specification (page 7) states that "A dropoff of 1.5 in the MLS score on either side of the peak MLS defines the are in which we can be 95% confident the gene resides. A dropoff in the MLS of 2 on either side of the peak is observed in a 20-cM region encompassed by D4S414 and D4S1611". Further, it is generally accepted in the art that LOD scores of 3.0 and above are indicative of linkage. Accordingly, a comparison between a DNA fragment of a test individual and an individual at least 98 years of age wherein the DNA fragment consists of a nucleotide sequence within the region flanked by markers D4S1564 and D4S1572 would provide information regarding the inheritance of a genetic marker linked with longevity and could be used in a diagnostic method to

predict the likelihood that an individual has an increased propensity for longevity. However, the specification does not teach what level of identity must be shared between the regions of D4S1564 and D4S1572 in order to indicate that an individual has a propensity for longevity. The specification teaches only that when the sequences are identical between sibships that one can conclude that an individual has a propensity for longevity. There is no guidance provided in the specification as to what level of sequence identity between the patient and individual samples is critical to determine propensity for longevity. It is unclear as to which sequences between the region of D4S1564-D4S1572 may be varied and which are not important in determining propensity to longevity. It is unclear as to whether patient fragments of the region of D4S1564-D4S1572 sharing only 10% or 20% or 50% identity with fragments for an individual at least 98 years of age would be useful for determining propensity for longevity. Additionally, the claims as broadly written appear to include methods in which polymorphic variants within the region of D4S1564-D4S1572 are identified and used to determine an individuals propensity for longevity. However, the specification has not identified any particular polymorphic variants within the region of D4S1564-D4S1572 which are correlated with longevity and thereby has not sufficiently enabled methods for predicting propensity for longevity by detecting polymorphic variants. The identification of a specific polymorphic variant, whether it be a variant of a genetic marker or an allelic variant of a gene, can only be determined through extensive experimentation. Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue

experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". In the instant case, the state of the art of identifying polymorphic variants correlated with specific conditions, particularly conditions as complex and broad as longevity, is highly unpredictable. Clearly, extensive experimentation would be required to identify a particular polymorphic variant that could be used to directly detect whether an individual has a propensity for longevity or resistance to age-related diseases. Additionally, extensive experimentation would be required to determine what level of sequence identity must be shared between 2 segments flanked by D4S1564 and D4S1572 in order to draw the conclusion that a patient has an increased propensity for longevity. In view of the high level of unpredictability in the art and the lack of guidance provided in the specification, undue experimentation would be required for one of skill in the art to practice the invention as it is broadly claimed.

3. Claims 15-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification as originally filed does not provide support for the concept in newly added claims 15-22 of a method in which the propensity for longevity is determined "based upon **an identity** between said segment obtained from said patient and said segment obtained from said individual who is at least 98 years of age." The specification as originally filed discloses methods in which a propensity for longevity was evaluated by identifying "chromosomal regions **that were identical by descent in the sibships**" (see page 7). However, the specification does not provide support for the broader concept of comparing DNA segments between a patient and any individual at least 98 years old and determining propensity for longevity based on any level of identity (e.g., 1% to 99% identity) between the compared DNA segments.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703)-308-1152. Papers related to this application may be faxed to Group 1634 via the PTO Fax Center using the fax number (703)-872-9306 or (703)-872-9307 (after final).

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196. .

Carla Myers

December 16, 2002

Carla Myers

CARLA J. MYERS
PRIMARY EXAMINER